



## Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at <http://about.jstor.org/participate-jstor/individuals/early-journal-content>.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact [support@jstor.org](mailto:support@jstor.org).

## THE TREATMENT OF GONOCOCCUS ARTHRITIS BY INJECTIONS OF DEAD GONOCOCCI, AND THE CLINICAL REACTION WHICH FOLLOWS THE INJECTIONS.\*

E. E. IRONS.

(*From the Memorial Institute for Infectious Diseases, and the Presbyterian and Cook County Hospitals.*)

It is now quite generally recognized that the course of certain infectious diseases may be favorably influenced by the subcutaneous injection at suitable intervals of small quantities either of the dead culture of the infecting organism, or of its products. This method of therapy is still in the early experimental stage, especially in diseases other than tuberculosis, and many observations will be required before we can form any definite conclusions as to its value. Infections by the colon bacillus, the staphylococcus, and the streptococcus have been treated by the subcutaneous injection of dead cultures often with apparent benefit, but by far the most extensive work along this line has been done with tuberculin in tuberculosis, in which the results have been on the whole encouraging.

The effect of the treatment of gonococcus infections by the injection of suspensions of dead gonococci has been recorded by a number of observers. Gonococcus vulvo-vaginitis has been treated by this method with varying success. Some workers have seen somewhat favorable results in the shortening of the duration of the discharge, while others have been able to detect no difference in the course of parallel series of cases, with and without the use of inoculations. A number of cases of acute urethritis in adults have been treated by killed gonococci, but in general the results obtained so far have not demonstrated any marked clinical value in this class of cases.

Relatively few cases of gonococcus arthritis and periostitis treated by inoculation have so far been recorded. Cole<sup>2</sup> and Meakins reported 15 cases of gonococcus arthritis in which inoculations were given and systematic observations made upon the opsonic index. After a careful study of the cases they concluded that inoculation of dead

\* Received for publication April 14, 1908.

<sup>2</sup> *Johns Hopkins Hosp. Bull.*, 1907, 18, p. 223.

gonococci appeared to have a decided value in favorably influencing the course of the disease.

The lesions which occur in the course of generalized gonococcus infections present certain characteristics which render these cases peculiarly favorable for the observation of the clinical effects of therapeutic injections of dead cultures of gonococci. The course, even in the acute cases, extends over a number of days at least, and much more often over weeks and months. The fever and other constitutional disturbances are relatively less than in other infections of corresponding extent in the body, and the lesions, involving chiefly the joints, tendons, and periosteum, are readily accessible to examination and careful observation.

In the course of the observations upon which this paper is based, 40 cases of gonococcus infection have been studied, including 31 cases of arthritis. The diagnosis of each case included in the series was determined beyond any reasonable doubt, from the clinical history and course as well as from the associated genital infection. In all the cases in any way obscure the diagnosis was confirmed by the isolation of the gonococcus from the joints, and in two cases from the blood.

In this connection it may be noted that there are many cases of obscure joint, periosteal, and synovial disease to which the term "chronic rheumatism" is applied, in which the gonococcus is the etiological factor. The remoteness in point of time of the primary infection, the peculiar clinical manifestations of the disease often simulating other affections such as tuberculosis, arthritis deformans, or other chronic arthritic or muscular diseases, the occasional extreme latency of the infection which becomes localized in some point of slight recent trauma with no detectable constitutional disturbance, and the tendency of physician as well as patient to regard an apparently healed gonococcus urethritis as a closed incident, all combine to cloud the diagnosis in these cases.

#### CULTURES USED FOR INOCULATION.

Bacteriologists are by no means agreed as to the relationship of the gonococcus to the meningococcus and other gram-negative diplococci, nor indeed as to the extent of the variations which occur in the various strains of the gonococcus. In working with a number of

cultures of the gonococcus, certain slight variations in cultural characteristics are observable, even in cultures of approximately the same age, and in the older cultures a gradual adaptation to growth on less highly albuminous media is frequently seen. Teague and Torrey in a recent study of the inter-relations of seven strains of gonococcus by means of the "fixation of complement" find marked differences in the immune sera obtained by the injection of the several strains into rabbits.

These and other similar facts have an evident bearing on the treatment of gonococcus infections by inoculation. In order that the inoculation treatment may have a general practical clinical value in the event of the experimental results receiving further confirmation, the dead cultures must be prepared, at least for the present, from heterologous organisms; for in many cases it is not only impracticable but impossible to obtain the so-called homologous strain.

Accordingly, for purposes of uniformity, all the cases in this series were treated with cultures obtained from other sources than the patients in question. The cultures of the gonococcus used were isolated from various lesions including urethritis and arthritis. As is well known, difficulties arise in the cultivation of the gonococcus which do not occur in the case of streptococci and staphylococci. Freshly isolated cultures of the gonococcus are often cultivated with difficulty; older cultures, however, usually grow readily, particularly on the more highly albuminous media such as ascites- and blood-agar.

If care is taken to transfer the cultures before the surface of the medium becomes dry, the organisms can usually be kept alive. Thus one strain has been preserved for 18 months and another for 12 months. However, in the preparation of material for inoculation, the more recently isolated strains have been used, preferably when from two weeks to three months old.

To obviate, in part at least, certain objections to the use of heterologous organisms, some of the material was prepared from two and sometimes three strains of the gonococcus. In many cases, however, but one strain was used. In a clinical study of this nature it is a matter of extreme difficulty adequately to compare the results obtained with different kinds of killed gonococci. The general impression is

that the immunizing responses were as good when one strain was used as when two or three were combined.

In preparing the killed gonococci the surfaces of large tubes of ascites- or blood-agar were inoculated, incubated for 24 to 48 hours, the growths then washed off with small quantities of salt solution, and the resulting suspension heated for one hour at 60° C. The number of organisms in the suspension was estimated by Wright's method, and also by employing the ordinary apparatus used in making a blood count. In the latter method the same line of procedure is followed as in making a red-blood count. Toisson's solution containing somewhat more methyl violet than usual is carefully filtered and used as the diluent. If a thin cover-glass is applied to the counting chamber, the stained organisms are readily distinguished with No. 7 Leitz objective. With care in agitating the pipette, a uniform distribution of the organisms can be obtained.

Lysol in salt solution was added to the suspension in sufficient quantity so that the final product consisted of a suitable number of organisms suspended in a solution of  $\frac{1}{4}$  per cent lysol. The dilution of the suspension was so gauged that the volume of the dose to be injected was from  $\frac{1}{2}$  to 1 c.c. Finally sterility was determined by cultures.

In the early cases treated, from 20 to 50 million organisms were given at a dose. A dose of this size usually produced a rise in the opsonic index, but often no coincident change occurred in the clinical course of the disease. It seemed advisable to increase the dose, and accordingly in the later work, from 100 to 500 million organisms were given. The intervals between injections varied from three to seven days.

#### THE OPSONIC INDEX.

The gonococco-opsonic index in 15 cases of gonococcus infection was studied with a view to determining its range and the fluctuations which may occur spontaneously and in response to treatment. In arthritic cases, the index before treatment was usually less than 1.0. A case of extensive arthritis gave indices of 0.6 and 0.9, a second case 0.5 and 1.1, a third 1.1, 0.8, and 0.8. In two other cases of somewhat less severe arthritis preliminary indices of 1.6 and 1.3, and of 1.3 were obtained. The average index of the arthritic cases

examined before treatment was 0.8. The more severe cases gave the lower average indices. In three cases of urethritis, without demonstrable metastatic lesions, the indices were 1.1, 1.1, and 1.2; 1.4 and 1.7; 1.5, 1.3, and 1.4 respectively. The injection of dead gonococci was followed usually by a sharp rise, the index sometimes reaching 2.5 or 3.0, with an average of from 1.5 to 2.0. Occasionally the rise was preceded by a slight fall. Similar observations have been made by other observers, and the results are cited here in further confirmation only of the general proposition that in gonococcus infection, as in other infections, the opsonic index shows certain characteristic variations, being often depressed during the course of the infection, and usually raised by the injection of suitable doses of dead cultures of the organism concerned.

Aside from the injection of dead gonococci, there are of course other factors which may cause fluctuations in the opsonic index. A patient with gonococcal prostatitis and a chronic urethral discharge received massage of the prostate. His gonococco-opsonic index as determined on five preceding days was 0.8, 0.8, 1.2, 0.8, 0.9. On the next day the prostate was massaged, and the following day the index was found to be 2.3. A week later, after the index had returned to 1.2 the prostate was again massaged, and 18 hours later the index was 2.9. Another patient suffering from gonococcus arthritis received massage of one of the knees involved, with a resulting definite rise in the opsonic index. Like observations have been made by Wright and others in various other infections, the specific opsonic index rising after exercise of joints, massage, the application of bandages to infected parts, etc.

Spontaneous fluctuations in the index also occur. Thus the index in a case of gonococcal epididymitis was determined for a number of days before treatment was begun. It was found to range between 1.0 and 1.3, and then suddenly rose to 2.9, falling 2 days later to 1.4, but with no corresponding variation in clinical course. The index in a case of arthritis was 0.8 on two successive days, and two days later without assignable cause it rose to 1.8. It is of course recognized that the technic of the determination of the opsonic index involves a certain margin of error, varying to a considerable extent with the skill and experience of the worker, but this margin of error

can hardly account for some at least of the fluctuations occurring in an otherwise regular series of gonococco-opsonic determinations. It seems probable that the explanation may be some accidental trauma or motion of joints, etc., similar in effect to massage of prostate or joints which we know at times produces just as marked rises in the opsonic index as does the injection of dead organisms. Owing to the localization of the infection in the joints which are necessarily exposed to more or less trauma, there is more likelihood in gonococcus arthritis than in at least some of the other infections of the occurrence of fluctuations in the index which cannot be correlated with the results of treatment, and which at times would be confusing if the opsonic index alone were the guide to treatment. The opsonic curve is the expression of only one of the many changes which may take place in the body fluids in response to infections.

Taking these facts into consideration, and bearing in mind that for some time at least inoculation therapy will depend for its control largely on clinical observation, it seemed advisable in the present work to use the clinical manifestations as the guide to the size and interval of the injections.

#### THE GONOCOCCUS REACTION.

In the following the clinical course of the cases under inoculation treatment, daily records of both subjective and objective conditions were made in so far as this was possible. It soon became evident that the course of events following the inoculation was not always one of progressive improvement. When seen 24 hours after the injection, patients repeatedly complained that the joint pains were worse rather than better. At this period of the work, the dose used was relatively small, and the exacerbation of the symptoms did not occur regularly after each injection, so that for a time, the phenomenon was regarded as an accidental coincidence. When the initial dose was increased, however, it was found that frequently the patients suffered from increased articular pain and tenderness after the first, often after the second, and occasionally after subsequent injections. Four cases in the same ward were given their first injections on the same day, the dose being 500 million. On the following day two of the cases showed only a slight increase in symptoms with some rise in temperature, and

pain in the joints. In these two, the arthritis was not extensive. In the other two cases in which the joint involvement was greater, there was a decided exacerbation of symptoms. The involved joints became more acutely tender, and the fever which had previously not exceeded  $99^{\circ} 5$  F. rose to  $101^{\circ} 5$ , associated with general malaise. On the second day after the injections, the acute symptoms had subsided and the patients felt about as well as before the injections were given. During the succeeding days improvement was more rapid than before the injections, so that the net gain of the first week of treatment was greater than that of the week preceding. In these cases the clinical picture after injection was most striking, and was highly suggestive of the phenomena observed in the tuberculin reaction.

The clinical records of the cases treated before this observation was made were now examined, and in those in which daily records had been made it appeared that the characteristic reaction had occurred though by no means to so great a degree. In subsequent cases, it usually has been possible so to graduate the dose of gonococci as to produce the reaction at will.

A typical gonococcus reaction is characterized by a rise in temperature, often only slight, an increase in pain and tenderness in the affected joints, with occasionally some increase in swelling, and a variable degree of malaise. The symptoms follow the injection in from 8 to 12 hours, and commonly last about 24 hours. Frequently there is a decided tenderness at the site of the injection, greater than occurs after the inoculation of the same dose of the same preparation in normal subjects. Occasionally there is marked redness and edema lasting from 24 to 48 hours. In a case of periurethral abscess of gonococcal origin without secondary infection which was under surgical treatment with drainage, an injection of 500 million cocci was followed in 18 hours by a moderate swelling and tenderness at the site of needle puncture, and also a marked increase in redness and tenderness about the wound. There was no coincident retention of pus, or local secondary pus infection to account for the phenomenon, and the wound returned to its normal condition in 24 hours. There is usually a slight increase in leucocytosis in the first 24 hours after injection.

The degree of the reaction is influenced by several factors. After



small doses (20–50 million in the cases in question) the reaction was not marked, and in a number of the early cases treated, it either did not occur or at least was overlooked. In one case (case 1), however, in which a 50 million dose was given, there was a reaction after each of the first three injections. When, beginning with a small dose, gradually increasing doses were employed, the reaction did not appear so typically, or was scarcely observable. When in a given case the same moderately large dose (300–500 million) was used for all the injections, the reactions became less with each injection. In four instances the reaction followed the initial dose only.

The most constant feature of the reaction is the increase in joint pain and tenderness. The temperature rise is often so slight as of itself to excite but little remark, especially in those cases in which there is a daily temperature of  $99^{\circ}5-100^{\circ}$ . In opsonic terminology, the clinical reaction corresponds to the negative phase.

#### THE AMOUNT INOCULATED.

In the absence of definite knowledge as to the relative value of various strains of the gonococcus for producing immunizing responses, it is not possible to set any arbitrary number of killed gonococci as the proper dose to employ. Cole and Meakins used from 300 to 1,200 million. The dose employed by several workers in the treatment of vaginitis in children is much smaller (10–50 million). For adults a small dose might be placed at 50 million, a medium dose at 300–500 million, and a large dose at 1,000 million. In determining the dose for any particular case, the general condition of the patient, and the extent of the arthritis must be taken into account. The dose of 500 million in the two extensive cases cited above was apparently too large, whereas in the less extensive cases it proved to be quite harmless.

The best results as to treatment in this series were obtained when the initial dose was just large enough to produce a slight clinical reaction, and the subsequent doses increased gradually. In no case was there any evidence that harm followed a moderate reaction.

#### CLINICAL RESULTS.

The clinical course of gonococcus infections is extremely variable. The large majority of the arthritic cases recover spontaneously, though frequently convalescence is long and tedious, and the patient may be

partially disabled for months. A periostitis of the os calcis, or a chronic peri-arthritis of the wrist, though relatively slight, may totally incapacitate the patient for work. It is obviously fallacious to draw conclusions as to the value of a treatment from the observation of isolated cases, and even when a number of cases of a disease so variable in its course as gonococcus arthritis are grouped together, one must be very guarded in the conclusions as to the rôle of the treatment in effecting a cure.

In summarizing the results, the previous duration of the arthritis, its course in the days or weeks immediately preceding treatment, and the rapidity of subsequent improvement are of greater weight than the mere statement of the time required to effect a cure.

In general, inoculation gave better visible results in the chronic than in the acute cases. In several of the acute cases improvement was apparently more rapid immediately following the injections than before. But, while the acute cases terminated favorably and without undue delay, it must be recognized that they might have done so without treatment, though possibly less rapidly.

The evidence in favor of the inoculation treatment is stronger in the subacute and chronic cases. In a number of cases in which after a typical acute course there remained more or less indolent swelling and tenderness in one or more joints, after the first injection the signs of the infection subsided rapidly. A patient (case 26) had had a typical gonococcus arthritis for 10 weeks. For six weeks before inoculation there had been no improvement in spite of rest and medicines. He was able to hobble around, but the pain in the lower dorsal region, sternoclavicular joint, and in the heels rendered him unable to work. After the slight reaction following the first injection of 300 million cocci his pain was much less, and after two more injections at intervals of four days he was discharged with no pain or other disability. When seen two months later he was still free from the trouble. A number of similar cases might be cited.

The treatment of several very chronic cases was undertaken. A patient (case 10) had suffered for years from recurrent attacks of "rheumatism" in the region of the lumbar spine and in the heels. For seven months, with the exception of one month, he had been unable to work. At one time the heels, at another the back seemed

to be the worse. He had taken medicines of many kinds, electrotherapy, etc., without benefit. The prostate was large, tender, and the fluid obtained by massage contained typical gonococci. Inoculation of dead gonococci was followed by an increase in pain and tenderness in the affected parts for 24 hours and then by improvement. After six injections during a period of one month, his condition was very much improved and he was able to go to work. Each injection was followed by an exacerbation of local tenderness. The subsequent improvement was much slower, but progressive. The injections were continued with increased dosage, combined later with massage of the prostate which was much less tender than at the outset of treatment. At the end of three months' treatment recovery was practically complete. The later injections were not followed by any observable clinical reaction.

In four of the 31 cases in the arthritic series, the results were unsatisfactory. Two of these (cases 18 and 22) were acute cases in which but two injections were given because of peculiar obstacles to treatment. These might reasonably be omitted from the series. Another subacute but extensive case (case 2) received only small doses (50 million) for one month without improvement, and the treatment was discontinued. Massage of the prostate was substituted, with subsequent recovery after a slow convalescence.

The fourth case was that of a chronic alcoholic, who had also a chronic nephritis with considerable edema. In addition to his gonococcus arthritis, he had an otitis media, and a dacryocystitis of a year's duration. Occasionally a slight reaction could be obtained after inoculation, with temporary improvement, but he suffered repeated relapses, with the involvement of new joints, and the treatment was finally discontinued.

The general impression derived from a study of the series of cases as a whole is that inoculation was of material value in hastening recovery. The evidence is strongest in the more chronic ambulatory cases in which the benefit of rest in bed can be eliminated.

Certain other general therapeutic measures also contributed to the favorable results. The repeated withdrawal of joint fluid in large recurring effusions was no doubt of value. Only the smallest degree of fixation of joints was used. There were no cases in which

ankylosis occurred. Prostatic massage has long been recognized as a valuable measure in gonococcus arthritis. It is highly probable on clinical grounds as well as from its effect in raising the opsonic index that prostatic massage results in an autoinoculation similar in its effect to the injection of killed gonococci. In several cases in which, for purposes of observation of the unaided effects of inoculation, systematic massage of the prostate was omitted, the condition of the prostate improved coincidentally with the improvement in the arthritis after inoculations.

#### THE CLINICAL GONOCOCCUS REACTION IN DIAGNOSIS.

As already stated the clinical phenomena which follow the injection of dead gonococci in patients suffering from gonococcus arthritis are in many respects similar to those which follow injection of tuberculin in cases of tuberculosis. The rise in temperature and malaise are relatively less in the gonococcus infections, but there occurs in addition an increase in symptoms in the joints. In some instances there is, too, a local reaction at the site of injection with tenderness, occasionally redness, and some edema. These local signs commonly subside in 24 hours, though in three cases they persisted for three or four days. Great care has been taken throughout to insure surgical cleanliness in the giving of the injections. Moreover, in a number of normal individuals, to whom the same amount was given, no local reaction was noted.

The frequency with which these clinical phenomena occurred suggested the possibility of utilizing the reaction in the diagnosis of obscure cases of arthritis in which the gonococcus was the suspected cause. The effects of the injection of dead gonococci into patients not suffering from gonococcus infection were accordingly studied. Eight adults in whom there was no history or sign of gonococcus infection were given injections of 500 million dead gonococci. In none of these was there any local change other than that following an ordinary hypodermic puncture, and no fever or constitutional disturbance was observed. In a case of pyorrhea alveolaris with subsequent general infection, and painful swellings over the extremities, there was no increase of fever or local symptoms following the injection. A case of gout with active joint involvement showed no local or general change after a dose of 500 million. Leucocytes before

injection 13,200; 18 hours after injection 13,000. Temperature normal throughout. A case of articular rheumatism showed no reaction, after 500 million. There was no increase in leucocytosis and the temperature chart showed no abnormal variations. A case of acute arthritis with pericarditis was thought possibly gonococcal in origin. There was no reaction after a dose of 500 million. Cultures from the blood and from a small amount of clear fluid aspirated from the knee remained sterile and the prostatic fluid contained no gonococci. The subsequent course was typical of acute rheumatic fever. In four other cases of acute and subacute articular rheumatism there was no reaction after injections of 500 million cocci.

In a number of suspected gonococcus cases the reaction was of value in making an early diagnosis. A case of monoarticular arthritis with effusion in the knee in which gonorrheal infection was denied was given an injection of 500 million. The evening temperature, which had previously reached only 100, rose to 101.8 and the joint pains increased. The knee was aspirated and the gonococcus isolated in pure culture from the fluid. A case of chronic arthritis which had resisted all treatment was given an injection. A slight rise in temperature with some increase in joint pains followed. The prostatic fluid was found to contain gonococci, and the subsequent course was that of gonococcus arthritis. A patient who had suffered from extensive gonococcus arthritis had been bed-ridden for one year. There was practically no motion in the knees. After an injection of 500 million the temperature which for weeks had been normal rose to 99.5, and the patient complained of malaise and increased pain in the joints. A patient with aortic aneurysm, who denied gonorrheal infection, had been selected for control experimental inoculations. After an injection of 500 million cocci, the temperature which had been uniformly normal, rose to 100° F. without any other apparent cause, returning to normal next day, with no subsequent rise. The prostate was examined and found to be large, somewhat tender, and the secretion contained numbers of leucocytes with typical intracellular gonococci.

#### SUMMARY.

Systemic infections by the gonococcus tend to spontaneous recovery. In many of the cases of gonococcus arthritis, the clinical

manifestations are acute, and the course extends over a few days or weeks. Certain cases, however, do not recover so quickly, and the condition passes into a chronic stage which may last months or years. In the first class of cases immunity develops rapidly, and clinically little benefit appears to result from the injections of dead gonococci. In the chronic cases, the mechanism of immunity fails to rid the body of the organisms, and they persist either in the original lesions or in one or more foci such as the prostate and give rise from time to time to new lesions at various points of localization. When dead gonococci are injected a reaction frequently follows with an increase in constitutional and local symptoms. This reaction is later followed by a period of improvement. The fact that with a dose of constant size, the reactions become less with each injection would seem to be a strong argument in favor of the value of the injections in hastening the development of immunity. Clinically in a number of cases the injections of dead gonococci have seemed to be of distinct value.

Many more series of cases must be studied before a definite opinion can be expressed, but the results obtained thus far seem to indicate that in certain cases at least of gonococcus arthritis recovery can be hastened by the injection of dead gonococci. No harm has appeared to follow the injections, and it is possible that the use of larger doses will be found desirable in some cases.

With further work the limitations as well as the advantages of the method will appear, and it should be recognized, that, while it is attractive theoretically as a specific therapeutic measure, too much must not be expected of it in the way of marvelous cures. It should be used rather in conjunction with other general measures such as rest, aspiration of joints distended with fluid, massage of the prostate, and other surgical and general hygienic treatment.

The reliability of the clinical gonococcus reaction as a diagnostic procedure will also be determined only after many tests. It has many points in common with the tuberculin reaction, and similarly too, there may well be cases of gonococcus infection found which do not respond. It appears, however, to be well worth a trial. Should the reaction prove to be reliable, a valuable and much-needed aid will be at hand for the diagnosis of obscure joint, synovial, and periosteal diseases.

Until recently it has not been deemed expedient to carry on in experiments on certain other phenomena of hypersusceptibility gonococcus infections such as the ophthalmic reaction, though this work has now been begun. It has already been noted that the local reaction after the injection of dead gonococci is greater in cases of gonococcus infection than in normal individuals.

I am greatly indebted to Dr. Hektoen of the Memorial Institute for advice and guidance during the preparation of this paper, and to the attending and house staffs of the Presbyterian and Cook County Hospitals for the opportunity afforded to observe clinical cases and for assistance in carrying out the treatment. I wish also to acknowledge the valuable assistance of Drs. A. H. Curtis and R. C. Menzies of the County Hospital who devoted much time and care to the daily observation and recording of the clinical phenomena of the cases in their charge.

Abstracts of the clinical histories of several of the cases are appended for the purpose of illustrating the phenomena observed during the course of the treatment.

The principal facts in the arthritis cases are summarized in the table. In a number of the cases, particularly the earlier ones, the records were not definite as to the occurrence of a reaction after the injections, and in these instances the fact is indicated by a dash (—) under the heading "Clinical Reaction."

The duration of treatment as given in the table comprehends the time elapsing until recovery was clinically complete, or until the patient passed from observation, in which event note of the fact is made.

#### ABSTRACTS OF CASES.

CASE 1.—M. S., female, white, *aet.* 27, actress; entered the hospital March 30, 1907, complaining of pain in the left knee, both ankles, left hip, elbows, right wrist, and right thumb.

The following history was obtained: Fifteen months ago the patient had severe pain and swelling in left knee joint lasting one month, associated with slight fever. Two months later a pelvic abscess formed and was drained.

Four weeks ago the patient fell, striking upon the left knee, but, aside from slight tenderness, suffered no inconvenience until one week ago when the knee became swollen and acutely painful. This was followed by pain and some swelling in both ankles, left hip, elbows, right wrist, and several of the small joints of the right hand. There had been only slight fever, no sweating, and no other marked constitutional

disturbance. Previous to marriage the patient was in good health. No history of rheumatism or other infectious disease. Following her marriage 8 years ago, the patient had 2 miscarriages, at 4 and 5 months, 1 full-term child, who has always been delicate, 1 miscarriage, 1 full-term healthy child, 1 miscarriage. No history of rash or other specific lesions. No further history of blennorrhagic infection could be obtained from the patient.

Physical examination showed a fairly well-nourished young woman. Nothing of note was found in the head, neck, or chest. The heart outlines and sounds were normal. The upper abdomen was normal. A vaginal examination showed dense bilateral pelvic adhesions, but no pus focus or tenderness was made out. There was a slight leucorrhea but careful search revealed no gonococci in the discharge.

The left knee was held in partial flexion, and there was marked tenderness and some swelling and redness in the popliteal space and over the inner flexor tendons. No effusion in the joint. The right wrist was slightly swollen, reddened, and exquisitely tender. There was pain on motion in the ankles, left hip, and in the elbows. The interphalangeal joint of the right thumb was painful, slightly swollen, and red.

A blood examination showed 4,160,000 red cells, 12,000 leucocytes, and 67 per cent hemoglobin (Dare). The urine contained a few leucocytes, but otherwise nothing abnormal was noted on careful examination.

On admission the patient was given salicylates by the house physician, and the affected joints partially fixed by soft bandages. Four days later the salicylates were stopped and the patient given potassium iodide gr. x and mercury binioidide gr.  $\frac{1}{10}$  three times a day. Credé ointment was applied daily to the affected joints. Hot dressings were applied to the knee with some benefit in allaying the pain which was particularly severe at night. The evening temperature did not rise above 100° F. with a morning range of from 98° to 99°. There was no sweating and the constitutional disturbance was relatively slight compared with the local trouble in the joints.

Clinically the case appeared to be one of gonococcus arthritis. After 10 days' rest in bed under the above treatment there was very little improvement in the knee and wrist, the two joints most involved.

Gonococco-opsonic index April 5, 1.1; April 6, 0.8.

*April 10.*—Extreme tenderness with swelling over median aspect of knee joint, and in the popliteal space. Some swelling and pain on motion in right wrist. Pain on motion, slight redness and swelling of left shoulder joint. Maximum temperature for past two days 99° 8 F.

Gonococco-opsonic index, 0.8. A subcutaneous injection of 50 million dead gonococci (Preparation I) was made into the left arm.

*April 11.*—Some increase in tenderness and swelling in right wrist. Maximum temperature 100° 8 eight hours after injection. Opsonic index 1.2.

*April 12.*—Still pain and swelling in right wrist. Knee and shoulder somewhat better. Max. temp. 99° 6.

*April 13.*—Opsonic index 1.0. Leucocytes 18,500.

*April 15.*—Wrist still swollen and tender. Knee somewhat better. Opsonic index 1.1. Injected 50 million cocci (Prep. I). Max. temp. eight hours after injection 101° 2.

*April 16.*—Wrist more swollen and tender. Max. temp. 100° 8.

*April 17.*—Opsonic index 1.9. Wrist improving; no spontaneous pain. Knee and shoulder can be moved without pain. No swelling. Max. temp. 99° 8.



*April 19.*—Wrist again painful, with some increase in swelling. Max. temp. 99°0.

*April 20.*—Wrist about as yesterday. Some pain in knee. Opsonic index 1.5. Injected 50 million cocci (Prep. I). Max. temp. 99°2.

*April 22.*—Opsonic index 2.2. Considerable improvement in wrist. Can move fingers better than previously.

*April 24.*—Wrist better. Can move fingers easily. Knee joint can be moved without pain. General condition good. Max. temp. 98°8. Leucocytes 13,500. Opsonic index 1.2. Injected 50 million cocci (Prep. I). Max. temp. eight hours after injection 98°6.

*April 25.*—Practically no change in joints.

*April 27.*—Some stiffness in left knee, but no swelling nor tenderness. Is using right hand and wrist normally without pain.

*May 1.*—No trouble in any of joints. Injected 50 million cocci (Prep. I). Max. temp. eight hours after injection 99°0.

*May 4.*—Insisted on returning to work. Walked out of hospital in good condition without joint symptoms.

In this case the diagnosis of gonococcus arthritis was apparently confirmed by the clinical course, although the gonococcus was not isolated from any of the lesions. The infection was one of moderate extent and severity, and for the first ten days the joints did not materially improve with rest in bed and medicinal treatment. The strain of gonococcus used was isolated five months previously from a case of acute urethritis, and kept in culture by repeated transfers on ascites-agar. Following each injection there occurred a rise in the opsonic index, though the opsonic index determinations were not so frequent as could have been desired. After each of the earlier injections there was a distinct rise in temperature, followed a few hours later by an exacerbation in the joint symptoms. The clinical import of these phenomena was not fully recognized at the time, but later, on referring to the clinical record, they were seen to occur with considerable regularity. It is difficult to say in how great a degree recovery was accelerated by the use of the inoculations. It may be stated, however, that the course was shorter than one would expect in cases of like extent and severity.

CASE 3.—J. B., male, *aet.* 29, laborer.

*December 19, 1907.*—The patient applied for dispensary treatment, complaining of pain in the mid-dorsal region, tenderness and pain on motion in the left shoulder and right knee.

*August 13, 1907.*—Following exposure a urethral discharge appeared with dysuria followed in one week by pain in back, left shoulder, and right knee in rapid succession. There was fluid in the knee joint for three weeks. The patient was confined to bed for four weeks. The highest temperature was 100° F. For the past three months has been able to be up and about, but unable to work on account of stiffness and pain in the joints.

Two years previously had an operation for frontal sinus infection. Otherwise the previous history was unimportant.

On examination there was found marked tenderness in the left shoulder without swelling, and over the mid-dorsal vertebrae, with pain on flexion (present since onset of trouble). Tenderness and pain on motion in right knee, but no effusion. Heels tender on pressure. Tenderness on pressure over an area 1 cm. in diameter over the crest of left ilium, apparently in the periosteum. No urethral discharge. The prostate

was large, tender, and after massage a considerable amount of fluid was expressed, which contained leucocytes and intracellular gram-negative biscuit-shaped diplococci. Temperature 99°. Pulse 90. The urine obtained before massage of prostate was normal.

A diagnosis of gonococcus arthritis and periostitis was made and the patient was given a subcutaneous injection of 100 million cocci (Prep. V) on December 19. He was also given urotropin gr. v four times a day.

*December 23.*—Patient reported that on the day following the injection the pain in all the affected joints was worse but that on the second day there was considerable improvement. On examination the joints were found to be less painful than at the previous examination; no tenderness in the heels; the tender area over the left ilium had disappeared. The patient stated that there was a slight morning discharge. A simple tonic was substituted for the urotropin, and a subcutaneous injection of 300 million cocci (Prep. VI) was given.

*December 30.*—Patient reported that he was again worse for two days after treatment, but now felt so much better that he desired to return to work. Some tenderness in dorsal spine, and in left heel. Injected 300 million cocci (Prep. VIII).

*January 6, 1908.*—Reported only slight exacerbation of symptoms after injection. Occasional pain on pressure in left heel. Some stiffness in left shoulder but no pain on passive motion. Back still somewhat painful on forward flexion. Injected 300 million (Prep. X).

*January 16.*—No increase in symptoms after last injection. There was now no complaint of pain in any of the joints or heels. There was some soreness in the lumbar muscles but no tenderness could be elicited in the vertebrae on pressure or motion. Injected 300 million (Prep. X). The patient returned to work.

This patient had taken various medicines for rheumatism without benefit, and had been incapacitated for work for a period of four months. The duration of injection treatment was about four weeks. No attempt was made to place the affected joints at rest.

CASE 6.—H. H., male, *aet.* 38, cook. Illness began October 15, 1907, with pain and swelling of the left ankle. Two days later the left knee became swollen and extremely painful on movement. The pain and swelling in the ankle quickly subsided but the knee did not improve and the patient entered a hospital.

Previous to the onset of the arthritis the patient had a sore throat for two days. No chills and not much fever. There was a history of syphilis 14 years previously, with a subsequent alopecia. Gonorrhea four years previously with a discharge for four months but no apparent complications. Since then there had been no discharge. No other illness.

The left knee was greatly swollen and tender with but little redness of the skin. The swelling was due partly to fluid in the joint, but there was also considerable swelling of the periarticular structures. The other joints, including the left ankle, appeared normal. The prostate showed little if any enlargement, and was not tender. The prostatic fluid showed no abnormalities microscopically. The remaining physical examination revealed nothing of note.

Urine normal; blood: reds 4,100,000, hemoglobin 78 per cent (Dare); leucocytes 9,000.

The patient remained under hospital treatment for one month, with rest in bed, partial fixation of the knee by bandages, salicylates, iodides, and mercury. The

temperature ranged from normal in the morning to 99° F.—100° F. in the evening. During the last week of this period the temperature did not rise above 99° F., but there was no improvement in the condition of the knee.

*November 14.*—The prostatic secretion obtained by massage showed a few organisms which resembled gonococci.

*November 16.*—The knee joint was aspirated and 60 c.c. of cloudy yellow fluid obtained, which contained many polynuclear leucocytes, and a few diplococci. The gonococcus was obtained in pure culture from the fluid.

*November 20.*—One hundred million dead gonococci (heterologous) were injected subcutaneously. A slight rise of temperature followed; but no local reaction in the joint. Leucocytes just before injection 10,500; 18 hours after injection 13,500.

*November 25.*—Two hundred and fifty million cocci were injected. No reaction whatever was observed. There was very little change in the condition of the knee. Leucocytes just before injection 8,400. Leucocytes 18 hours after injection 9,500.

*December 3.*—Sixty c.c. of slightly cloudy fluid was aspirated from the joint. A few gonococci and many polynuclear cells were present in the fluid; 500 million cocci injected subcutaneously. No reaction was observed.

*December 10.*—The periarticular swelling had decreased, but fluid had reaccumulated; 60 c.c. of slightly blood-stained gelatinous fluid aspirated. This fluid was clearer than that from preceding aspiration. Five hundred million cocci injected (Prep. VI). Following this injection the evening temperature which had been 99° F. on two preceding days, reached 99° 8 F. on the two succeeding days. Seven days later the evening temperature was normal, the swelling of the knee was decreased, and the patient was able to walk without pain, although the motion was not as free as normal. The patient left the hospital and returned for inspection at intervals of seven days. He was given two more injections of 500 million (Prep. VI), Dec. 17 and Dec. 24.

*January 10.*—There was no swelling or pain in the knee, and motion was normal without stiffness. When last seen, January 20, there had been no recurrence of trouble.

The favorable result in this case was due in part, no doubt, to the repeated removal of the fluid from the joint, although the infection involved to an unusual extent also the periarticular structures. Throughout the treatment the joint was allowed free movement, no apparatus for fixation being used. Duration of treatment, 34 days.

The limitation of the infection to one joint probably accounted for the relatively slight reaction following the injections. A slight rise in the leucocytes, followed each injection.

CASE 7.—J. T., male, *aet.* 36, laborer. Patient came to the dispensary January 3, 1908, complaining of pain in left ankle and swelling and pain in the left knee. The pain was continuous and worse at night.

First had gonorrhea 14 years ago, followed three months later by "rheumatism" which involved the knees, hips, and ankles, and which lasted intermittently for two years.

*November 15, 1907.*—The patient had a recurrence of gonorrhea, and on December 1, began to have pain in the left ankle, followed in three days by swelling and pain in the left knee. Very little fever or constitutional disturbance.

On examination, the left knee was found greatly enlarged, due in part to periarticular swelling, and in part to a moderate joint effusion. Some swelling, redness, and tenderness were present over the left internal malleolus. No tenderness was elicited in the heels. A slight urethral discharge was present which contained typical intracellular gonococci. The prostate was normal in size and not abnormally tender; 120

c.c. of greenish-yellow cloudy fluid aspirated from the knee joint. Smears showed many polynuclear leucocytes, but no gonococci or other organisms were found. Cultures on ascites- and blood-agar remained sterile.

*January 3.*—A subcutaneous injection of 300 million cocci (Prep. VI) was given and the patient directed to take urotropin gr. v four times a day.

*January 4.*—Pain in the knee better (relieved by aspiration). Pain in ankle worse.

*January 6.*—Ankle some better but still tender. Knee less swollen and only moderately painful. 300 million cocci injected (Prep. X).

*January 9.*—Ankle more painful for 24 hours after last injection. Knee distended with fluid. Aspirated 120 c.c. of cloudy yellowish gelatinous fluid. 300 million cocci injected (Prep. X).

*January 13.*—Knee joint again distended with fluid. Aspirated 150 c.c. cloudy yellowish fluid from knee and a flannel bandage applied to joint. Ankle better. Very little swelling or tenderness. Urethral discharge decreased, but present; 300 million cocci injected (Prep. X).

*January 16.*—Knee much better; very little fluid, and not tender. Ankle which was worse for 24 hours after last injection slightly swollen and tender; 300 million cocci injected (Prep. X).

*January 20.*—No swelling or tenderness in knee. No increase in pain or swelling in ankle after last injection. Some tenderness and swelling still present in ankle. Some tenderness in left heel.

*January 23.*—Walked without cane. No fluid, tenderness, or stiffness in knee. Ankle completely recovered except for slight stiffness; urethral discharge had ceased; 500 million cocci injected (Prep. XI).

*January 30.*—No exacerbation of symptoms after last injection. A small amount of fluid present in knee; slight urethral discharge present; 500 million cocci injected (Prep. XI).

*February 6.*—No pain in joints. Knee and ankle freely movable; there was a slight increase in tenderness in ankle after last injection; 500 million cocci injected (Prep. XI). Also the patient was given 1 per cent protargol solution for urethral injection.

*February 13.*—The patient reported that he had returned to work and had no pain nor stiffness in any of his joints. Urethral discharge had ceased.

CASE 8.—J. M. C., male, *aet.* 36, cook. Gonorrhea first 15 years previously, with repeated subsequent attacks. Arthritis four years previously involving toes, ankles, and knees.

Present illness began two weeks previous to admission to the hospital with urethritis, followed one week later by arthritis involving successively, in order, the small joints of right hand, the right ankle, right knee, left shoulder, left great toe, left knee. When first seen, the patient had been under hospital treatment with rest in bed, iodides, and urethral injections for two weeks. The arthritis (of three weeks duration) had improved somewhat.

*November 13.*—The patient had become very thin during his illness. The left ankle was painful and swollen. Right wrist stiff and swollen. Tenderness and swelling in right knee and left great toe. Fluid in left knee; heels tender; prostate enlarged and tender. A smear from urethral discharge after prostatic massage showed typical intracellular gonococci. Injected 500 million cocci (Prep. VI).

*November 14.*—Pain in joints worse. Marked malaise. Slight rise in temperature.

*November 15.*—Joints still painful but some improvement.

*November 17.*—Joints showed marked improvement. Fluid in knee decreased.

*November 23.*—Improvement had been slow but continuous to this date. Knees and ankles still somewhat tender. No fluid. Tenderness but no swelling in right elbow and in shoulders. Some swelling over dorsum of both feet. Injected 100 million cocci (Prep. VI).

*November 26.*—Much better. Able to get up and move about ward. No reaction after last injection.

*November 27.*—Injected 300 million cocci (Prep. VI).

*November 30.*—Still some stiffness in right knee and right wrist. Injected 500 million cocci (Prep. VI).

*December 1.*—Involved joints sore and stiff. From this point on improvement was rapid. An injection of 300 million cocci (Prep. VI) was given on December 8. On December 10 there was no pain or tenderness in any of the joints, and the only complaint was of stiffness on attempted movement. No limitation of passive motion. The patient remained in the hospital 16 days longer and gained rapidly in weight and strength. On December 29 he reported for inspection. No limitation of motion or tenderness in any of the joints. Two months later the patient reported that he was in good health and that all the joints were normal.

In all, this patient received five injections. The duration of treatment was four weeks. The first injection of 500 million cocci was followed by a marked clinical reaction, with exacerbation of joint symptoms, malaise, and some fever. The arthritis was extensive and the patient showed the effects of prolonged illness by his emaciation. The dose in this instance proved to be too large as the degree of reaction was greater than was desirable. Subsequent smaller doses were not followed by marked reaction though the joints showed some increase in tenderness following a second later injection of 500 million cocci.

CASE 9.—A. C., male, *aet.* 37, laborer. Entered the hospital complaining of pain and swelling in the left knee, which had been present for two weeks. Denied gonorrheal infection. A slight urethral discharge showed no organisms. The periarticular structures of the left knee were greatly swollen and tender. Fluid was present in the joint. Prostate normal in size and not tender. After two days' rest in bed there was no improvement. Following the injection of 100 million cocci (Prep. VI) the evening temperature which had previously been 100° F., rose to 101° 8'. Three days later a second injection of 300 million (Prep. VI) was given, and next day 25 c.c. semipurulent yellowish fluid was aspirated from the joint. The gonococcus was obtained in pure culture from the fluid.

Five more injections of 100, 150, 300, 300, and 500 million respectively were given at intervals of five days, each injection being followed next day by the aspiration of fluid from the joint. No rise in temperature followed the later injections.

The patient was discharged with good motion of the joint without pain or swelling. Duration of treatment 30 days. Incision and irrigation of the joint were considered, but the result justified the more conservative course.

In the light of previous cases, the rise in temperature following the first injection favored the probable diagnosis of gonococcus arthritis, which was later confirmed by cultures.

CASE 10.—E. G., male, *aet.* 36, machinist, single. When first seen in the office October 21, 1907, the patient complained of tender heels, pain and stiffness in the dorsal spine, and tender points over the right tibia just below the patella, the crest of the left ilium and in the right sacroiliac region.

The following history was obtained. With the exception of typhoid fever 18 years ago, the patient has suffered from no severe illness. No syphilis. Had an attack of gonorrhea 14 years ago, with a discharge for two weeks, followed by a recurrence soon after, the discharge persisting for five weeks. No arthritis.

Six years ago the patient suffered from pains in the dorsal region, particularly on bending over. This was worse in the morning and improved after moving about for an hour or so. The pain and stiffness in the back continued at intervals, with periods of remission until April, 1907, when he had a urethral discharge which disappeared after two days and has not been present since. He insists that there was no possibility of exposure to fresh infection. Immediately following the discharge the left heel and left hip became painful. Soon after, the right heel became tender. He was partially disabled for several weeks, and then returned to work. A month later the ankles and heels became painful, but there was very little swelling and no redness. The temperature and pulse were normal, and there was no other constitutional disturbance noted. A diagnosis of flat foot was made and the patient was given steel arches with but little resulting benefit. Three months ago he began to have pain in the left hip, extending down the back of the leg. This continued for two months and one month ago he entered a hospital where a diagnosis of sciatic neuritis was made. He received no benefit from two weeks' treatment.

During the course of his illness the patient had remained in good physical condition, but for seven months had been incapacitated for work, with the exception of a short time soon after the onset. He was an intelligent man, and while discouraged by his prolonged disability he was not neurotic, and did not magnify his symptoms. He had received many kinds of treatment, including electricity, thermotherapy, salicylates, iodides, and mercury. He was temperate in the use of alcohol and tobacco.

The physical examination showed a well-nourished young man, of medium height. Nothing abnormal was noted in the chest or abdomen. Both heels were very tender on pressure, but there was no swelling or redness. A tender area 1 cm. in diameter was present over the left tibia just below the insertion of the patellar tendon, with apparently a slight thickening of the periosteum. A small tender area was present in the right sacroiliac region which seemed to be in the fascia rather than in the bone or joint. Over the lower dorsal vertebrae there was tenderness on deep pressure on the spinous processes, but no lesion of the bodies of the vertebrae could be made out. There was no urethral discharge. The prostate was uniformly enlarged, rather firm and tender on deep pressure. An examination of the prostatic fluid obtained by massage showed a moderate number of leucocytes, a few typical gram-negative diplococci, both free and intracellular. Urine normal.

A diagnosis of gonococcus arthritis and periostitis was made and treatment by the injection of dead gonococci was begun. No other medication.

October 21.—Six hundred million cocci injected (Preparation VI) in right arm.

October 24.—The back was better, though still stiff. Tibia and heels as before. Soreness in the sacroiliac region had disappeared. The patient reported that for two days after the injection he felt worse. There was an increase in the pain and stiffness

in the back, and also a slight redness at the site of injection; 700 million cocci injected (Prep. VI).

*October 26.*—Not much change. There was very little increase in tenderness after last injection; 700 million cocci injected (Prep. VI).

*October 30.*—Slight increase in pain in tibia after last injection. This was somewhat improved. The back was still painful, but less so than before treatment; 750 million cocci injected (Prep. VI).

*November 4.*—Not much improvement since October 30; 500 million cocci injected (Prep. VI).

*November 11.*—Patient stated that he felt better than for seven months. The pain in the back though still present was much less and he could bend forward more easily. There was no increase in pain or tenderness after the last injection.

*November 15.*—Not so well. The left heel was tender, and there was pain in the back somewhat higher than before. The spine was only slightly tender on pressure, but there was some limitation of forward flexion on account of the pain. The prostate was somewhat tender and larger than normal. Prostate massaged.

*November 20.*—Back better. Still some pain in heel; 200 million cocci injected (Prep. VI).

*November 25.*—No reaction noted after last injection, 200 million cocci injected (Prep. VI).

*November 30.*—Two days ago the pain in the back was worse, but this disappeared in 24 hours and the patient reported that he felt better than at any time previously, and was able to return to work.

Up to this point the patient had improved steadily. The acute tenderness in the heels and back had decreased until the only complaint was that of slight pain in the morning on rising which disappeared in about two hours. The injections were continued at intervals of about five days, using an average dose of 300 million cocci for six weeks longer. At the end of this period there was only a very slight tenderness in the back. The prostate was still tender and the secretion contained a few gonococci. The injections were continued as before, and the prostate massaged. The improvement was very slow, but there was no relapse and by the middle of February the recovery was practically complete.

This case was of long standing and very stubborn. During the first month of treatment, the progress was satisfactory. It was a matter of much greater difficulty however, to get rid of the last traces of infection, particularly in the prostate, which seemed to be the focus of infection as is the case in so many of these patients. Massage of the prostate was purposely omitted during the early treatment, as it was desired to see to what degree the prostatic infection could be influenced by the injection of cocci subcutaneously. When prostatic massage was resumed, the prostate was smaller and much less tender than when treatment was begun, although there was some trouble remaining, as was evidenced by the presence of a few organisms in the expressed secretion. Throughout the course of treatment no constitutional disturbance was observed. Locally in the lesions, however, a distinct exacerbation of symptoms followed the injections. This reaction lasted 24 hours, and was followed by a period of improvement. The degree of the reactions became progressively less, though in this case an occasional slight increase in local tenderness occurred even after the later injections.

In point of the time required for treatment this case is not a brilliant example of the success of the therapy, though it seems not unreasonable to credit the method with

some part at least in the recovery. Throughout the treatment the patient led a normal life taking daily outdoor walks.

CASE 11.—O. H., male, *aet.* 25, laborer. Entered the hospital November 27, complaining of pain and swelling in the ankles and feet, of 10 days' duration, and of an acute urethritis, present for 5 weeks.

Five years previously had gonorrhea lasting five weeks, without complications. No other illnesses.

On examination the left foot was found swollen and tender, with some redness over the dorsum. Extensive involvement of the tarsal and metatarso-phalangeal joints. The right ankle, and right metatarso-phalangeal joint of the great toe were swollen and extremely tender. A purulent urethral discharge contained typical gonococci.

After three days' rest in bed the pain and swelling in the joints were no better. Two injections of 100 and 150 million cocci respectively at intervals of four days were followed by some improvement. After a third injection of 300 million four days later (December 8) there was a marked exacerbation of joint pain, lasting 24 hours, followed by a period of improvement. Two more injections of 500 and 300 million were given at intervals of seven days. The arthritis subsided slowly but steadily and the patient was able to walk without much difficulty by December 29. On leaving the hospital January 4 there was only a slight tenderness in the left foot.

The case was an acute one of moderate severity. Recovery, though occurring within a reasonable time, was not more rapid than seen in cases under other treatment, and could hardly be ascribed to the use of the injections. A decided reaction followed the third injection of 300 million cocci.

CASE 12.—M. F., male, *aet.* 38, engineer. Contracted gonorrhea 17 years ago, with subsequent attacks nine years, six years, and three years ago. Arthritis involving the ankles, right instep, both knees, and one finger followed the attack three years ago. The patient was sick for 14 weeks, and had to use a cane for a year afterward.

The present urethritis appeared October 2 and the arthritis October 9, involving both ankles and knees.

When first seen on November 13, the patient had been under hospital treatment with rest in bed for three weeks, without much improvement. Both ankles were swollen and tender; heels tender. Both knees painful on motion, with moderate effusion. Right sacroiliac joint tender. A typical purulent urethral discharge was present. Fever slight, normal in morning, occasionally reaching 100° F. at night.

*November 13.*—8 P.M.; 500 million dead gonococci were injected subcutaneously.

*November 14.*—Joints worse, acutely tender; general malaise with headache and anorexia. Temperature A.M., 100° F.; P.M., 101°.

*November 15.*—Better but still felt sick.

*November 16.*—Much better. Temperature P.M., 99°·6. Joints much less tender.

*November 17.*—Considerable improvement in all joints except right knee which contained a large amount of fluid. No fluid in left knee.

*November 20.*—No demonstrable fluid in knees. Left knee, ankles, heels, and sacroiliac joints showed some tenderness.

*November 23.*—An injection of 100 million cocci was followed by a slight increase in pain in the affected joints, but there was no rise in temperature.

*November 27.*—An injection of 300 million cocci was given with no marked increase in symptoms.



*November 30.*—One hundred million cocci injected. Some increase in stiffness in joints but no constitutional disturbance.

The patient at this time was emaciated and weak. The arthritis though still present was much less painful. Improvement was steady but slow. Injections were given as follows: December 4, 150 million; December 9, 300 million; December 13, 250 million; December 21, 300 million; January 7, 500 million. No observable reaction followed these injections. On December 4 the patient sat up in a chair, and on December 16 was able to walk about the ward with the aid of crutches. His appetite improved and he gained rapidly in weight and strength.

When discharged on January 10, the patient had good motion in all the joints. With the exception of a small tender area over the inner aspect of the left knee, there was no pain or tenderness present.

This case was extensive, with evidences of severe toxemia. The emaciation and weakness were pronounced. For three weeks prior to the inoculations there had been little improvement with rest in bed. The first injection of 500 million was followed by a decided reaction, and it was evident that a smaller dose would have been better. Later, when convalescence was established, a dose of 500 million was followed by no reaction whatever. Here, as in other cases, it is impossible to state the time which would have been required for recovery on other treatment. The injection of dead gonococci did, however, have a decided influence on the clinical course of the disease, as evidenced by the reactions, and when suitable doses were employed, the effect appeared to be not unfavorable.

TABLE I.  
SUMMARY OF CASES.

Case No.	Age	Sex	Joints Involved	Original Infection	Pre-vious Arthritis	Date of Appar-ent Re-fection before Present Arthritis	Dura-tion of Present Arthritis before Treat-ment	Inocula-tions Average Dose	Num-ber of Inocula-tions	Clini-cal Reac-tions	Dura-tion of Treat-ment	Result	General Treatment	Remarks
1	M. S. 27	F.	Knee, wrist, thumb	?	15 mo.	.....	2 wks.	50 mil.	5	3	24 days	Recovery	Rest in bed. Tonics	No improvement after 10 days' rest in bed prior to treatment. Rise in gonococ-coponic index, coincident with periods of improvement after inoculations
2	McC. 27	M.	Knees, ankles, shoulder	5 yrs.	.....	3mo.	10 wks.	75 mil.	6	3	1 mo.	No im-prove-ment	Rest in bed. Light flannel bandage to joints	Gonococcus obtained in culture from joint. No improvement with inoculations. Re-covered in 2 mos. with massage of prostate
3	J. B. 29	M.	Shoulder, dorsal vertebrae, knee, heels	4 mo.	.....	.....	4 mo.	250 mil.	4	3	4 wks.	Recovery	Placebo. Dispen-sary treat-ment. No fixation or rest of joints	Improvement rapid after injections. A chronic case, which had failed to im-prove after 4 mos. of other treatment
4	N. M. F. 29	M.	Sternoclavi-cular, finger foot, heels	4 yrs.	4 yrs.	1 week	10 wks.	60 mil.	2	—	14 days	Improved	Placebo.	Improvement. Returned to work
5	H. M. 26	M.	Sacroiliac, knee, an-kle, heel	3 yrs.	.....	1 wk.	10 days	400 mil.	2	—	7 days	Recovery	Dispensary. No fixation	An acute case. Recovery rapid. Rest in bed no doubt a large factor
6	H. H. 28	M.	Knee	4 yrs.	.....	denied	4 wks.	400 mil.	6	—	34 days	Recovery	Rest in bed	Gonococcus isolated from seropurulent joint fluid. Repeated aspiration of fluid from joint. No ankylosis
7	J. T. 36	M.	Ankle, knee	14 yrs.	14 yrs.	2 wks.	4 wks.	400 mil.	6	4	30 days	Recovery	Placebo. Dispensary treatment	Gonococcus in urethral discharge. Cul-tures from knee joint sterile. Repeated aspiration of joint. No ankylosis
8	J. M. C. 36	M.	Ankle, wrist, knees, toe, heels	15 yrs.	4 yrs.	1 wk.	3 wks.	300 mil.	5	4	30 days	Recovery	Rest in bed. Placebo	Some improvement with 2 weeks' rest in bed before treatment. Marked reactions to earlier injections
9	A. C. 37	M.	Knee	.....	.....	denied?	2 wks.	250 mil.	7	1	30 days	Recovery	Rest in bed. Placebo	Gonococcus isolated from seropurulent joint fluid. Repeated aspiration of joint
10	E. G. 36	M.	Vertebrae, heels, per-istitis of tibia, and ilium	14 yrs.	6 yrs.*	.....	7 mo.	400 mil.	20	7	3 mo.	Marked im-prove-ment	Placebo. Allowed regular out-door exer-cise	A chronic case. Rapid improvement for first month. Slow but progressive im-provement till recovery practically com-plete. Massage of prostate

TABLE 1.—Continued.

Case No.	Age	Sex	Joints Involved	Original Infection	Pre-vious Arthritis	Date of Apparent Infection before Present Arthritis	Dura-tion of Present Arthritis before Treatment	Inocula-tions Average Dose	Num-ber of Inoc-ulations	Clini-cal Reac-tions	Dura-tion of Treat-ment	Result	General Treatment	Remarks
11	O. H. 25	M.	Ankles, foot	5 yrs.	.....	5 wks.	10 days	250 mil.	6	2	34 days	Recovery	Light band- age. Rest in bed. Placebo. Rest in bed. Tonics	An acute case. Two well-marked clinical reactions following injections
12	M. F. 38	M.	Ankles, knees, wrists	17 yrs.	3 yrs.	1 wk.	6 wks.	250 mil.	6	4	50 days	Marked improve- ment	Rest in bed. Tonics	A very extensive case, with profound clinical reaction after first injection of 500 mil. General condition poor, and con- valescence slow. Final result good
13	J. McN. 22	M.	Spine, ankles, knees	4 yrs.	.....	6 mo.	6 mo. exacer- bation 10 da. 5 wks.	100 mil. 300 mil.	5	1	26 days	Recovery	Rest in bed	An acute exacerbation. Organisms iso- lated from fluid from ankle and from blood. No ht. lesion demonstrable. Marked reaction after 2d injection
14	F. S. 24	M.	Shoulder, ankle, knees, heels	6 wks.	.....	.....	.....	250 mil.	7	1	30 days	Recovery	Rest in bed 1 wk. pre- vious to treatment. Slight im- provement. Rest in bed. Placebo	A subacute case. No reaction after 2 in- jections of 100 million. A 3d injection of 300 mil., followed by a sharp rise in temperature 6 hrs. later, with some ex- acerbation of joint pain. Gonococci in prostatic fluid
15	J. M. 20	M.	Ankles, knees, me- tatarsals	5 wks.	.....	5 wks.	3 wks.	250 mil.	7	2	35 days	Recovery	No improve- ment with 2 wks. rest in bed previous to treatment	A subacute case. Patient in poor physical condition. Progress slow. Gonococci in urethral discharge
16	H. C. 35	M.	Knees, ankles, wrist, spine, heels	10 yrs.	7 yrs. 2 yrs.	.....	3 wks.	350 mil.	14	2 slight	3 mo.	No per- manent im- prove- ment	Partial rest. Tonics. Iodides without benefit	A chronic case; alcoholic; chronic nephri- tis with considerable edema; anemia; prostate large and tender; old history of syphilis; dactylocystitis 1 year; otitis media with onset of present arthritis. Several periods of improvement after in- jections of 500 million, followed by re- lapses. Gonococcus in prostatic fluid
17	C. K. 23	M.	Sacroiliac, knee, ankles	3 yrs.	3 yrs. 8 mo.	.....	3 wks.	150 mil. 500 mil.	4 4	0 1	20 days 20 days	Recovery	Rest in bed. Tonic	No response to treatment and no reaction during first period of 20 days using 100- million dose. When dose was raised to 500 million a slight reaction followed and improvement was steady. Gono- coccus isolated from knee-joint fluid

TABLE 1.—Continued.

Case No.	Age	Sex	Joints Involved	Original Infection	Pre-vious Arthri-tis	Date of Appar-ent Re-infection before Present Arthritis	Duration of Present Arthritis before Treatment	Inoculations Average Dose	Num-ber of Inoc-ulations	Clini-cal Reac-tions	Duration of Treatment	Result	General Treatment	Remarks
18	J. S. 40	M.	Ankles, spine, knee	3 yrs.	3 yrs. 1 yr	Continued gleet	6 wks.	400 mil.	2	—	10 days	Some im-prove-ment	Rest in bed. Urotropin, pot. iodide. Bier's hy-peremia Up and around ward	Some improvement following injections. Injections discontinued on account of excess of other treatment
19	W. E. 23	M.	Knees, an-kles, cervi-cal spine	4 yrs.	.....	3 wks.	9 wks.	400 mil.	2	—	5 days 10 days	Marked Im-prove-ment	Up and around ward	No improvement on rest in bed and salicylates for 6 weeks. Rapid improvement after 2 injections. Then passed from observation 10 days. When next seen had relapsed. Injections followed by 2d marked improvement
20	J. W. 28	M.	Knee, ankle	6 mo.	.....	6 mo.	3 mo.	400 mil.	2	—	7 days	Im-prove-ment	Rest in bed and salicylates for 1 wk. prior to injections, with some im-provement	Joints improved rapidly during week following injections
21	L. J. 25	M.	Ankle	7 wks.	.....	.....	5 wks.	50 mil.	3	—	11 days	Recovered	Partial rest	Was improving before treatment. Improvement rapid after injections. After injection the opsonic index rose from 0.9 to 3.2. Case passed from observation without clinical improvements
22	T. W. 25	M.	Ankle	10 wks	.....	.....	1 wk.	50 mil.	2	—	7 days	No im-prove-ment	Rest in bed	Patient improving when inoculations were begun. Opsonic index was 0.8, 1.6 on 2 days previous to 1st injection. After inoculation 0.6, 0.8, 0.7. Clinically progressively improving. After 2d injection index 1.1, 1.1
23	L. S. 18	M.	Ankles, knee	5 wks.	.....	.....	3 wks.	50 mil.	2	—	12 days	Recovery	Partial rest	Improving slowly up to time of beginning inoculations. Improvement more rapid after inoculations
24	P. B. 33	M.	Spine, knee, hip, tem-poro-maxil-lary, heels, finger	4 yrs.	.....	6 wks.	3 wks.	400 mil.	3	—	14 days	Recovery	Patient up and around ward	Patient improving before inoculation. No apparent influence on already favorable course
25	N. N. 19	M.	Shoulder	3 wks.	.....	.....	12 days	50 mil.	2	—	8 days	Recovery	Ambulatory	

TABLE 1.—Continued.

Case No.	Age	Sex	Joints Involved	Original Infection	Pre-vious Arthri-tis	Date of Appar-ent Infection before Present Arthritis	Dura-tion of Present Arthritis before Treat-ment	Inocula-tions Average Dose	Num-ber of Inoc-ulations	Clini-cal Reac-tions	Dura-tion of Treat-ment	Result	General Treatment	Remarks
26	P. M. 22	M.	Sternoclavi- cular, heel spine, knees, sacroiliac	4 mo.	.....	.....	10 wks.	300 mil.	3	1 slight	2 wks.	Recovery	Rest in bed	A mild but chronic case. A slight reac- tion followed first inoculation of 500 mil. Recovery apparently hastened by treat- ment
27	C. W. 25	M.	Knees, ankle, heels, spine	4 mo.	.....	.....	2 mo.	500 mil.	6	3	1 mo.	Rapid im- prove- ment	Rest in bed for 2 wks. Then am- bulatory treatment	Patient growing steadily worse at time was begun. Moderate reactions were ob- tained after the 1st two injections of 500 million cocci. Effusions in knee joints were aspirated as they recurred. The gonococcus was isolated from the joint fluid. Improvement was rapid after 2 injections and patient returned to work in 1 month, though there was still tenderness in one foot.
28	A. L. 21	M.	Foot, wrist, heels, toes	6 wks.	.....	.....	4 wks.	400 mil.	8	2	5 wks.	Steady im- prove- ment	Ambulatory. Placebo	The patient was incapacitated for work as ironer in laundry by arthritis in right wrist. No improvement for 3 wks prior to treatment. Returned to work in 16 days after beginning treatment (4 injec- tions). Injections continued with pro- gressive improvement. Gonococci in prostatic secretion. Massage of pros- tate on 3 occasions. Two reactions after injections. Later doses of 500 mil. gave no reaction.
29	J. D. 22	M.	Ankles, knees, sacroiliac, finger	4 wks.	.....	.....	1 wk.	500 mil.	19	2	2 mo.	Improve- ment	Rest in bed, sod, salicy- late gr. xv; sod benzo- ate, gr. v; q. i. d. for 2 wks.	An acute case, with complicating periar- thritis, pleuritis, and probable endocardi- tis. Gonococci in urethral discharge and isolated in culture from joint on 2 occa- sions. Blood cultures negative. Recovery. No apparent benefit from injections, though 2 reactions occurred after in- jections, with rise in temperature

TABLE 1.—Continued.

Case No.	Age	Sex	Joints Involved	Original Infection	Pre-vious Arthri-tis	Date of Appar-ent Re-infection before Present Arthritis	Dura-tion of Present Arthritis before Treat-ment	Inocula-tions Average Dose	Num-ber of Inoc-ula-tions	Clini-cal Reac-tions	Dura-tion of Treat-ment	Result	General Treatment	Remarks
30	M. N. 24	M.	Knees, ankle, toe, metatarsals, heels	2 yrs.	2 yrs.	?	10 wks.	500 mil. 200 mil.	4 11	1 slight	16 days	Improvement	Partial rest. Urotropin, gr. v, q. i. d.	Painful heels for 2 yrs. since initial arthritis. Acute exacerbation of arthritis for 7 wks. with urethritis. Some improvement with rest in bed for 10 days previous to treatment. Arthritis subsided rapidly after injections. On leaving hospital there was slight tenderness of one knee, and tenderness in heels persisted. The patient returned at intervals of 1 wk. for 10 weeks, receiving an average dose of 200 mil. At the end of this time, there was no demonstrable tenderness in the heels and the joints all appeared normal
31	C. A. 31	M.	Heels, back, acromio clavicular, perostitis of patella and tibia	6 yrs.	.....	.....	3 yrs. at intervals	300 mil.	..	—	3 mos.	Improvement	Ambulatory	A chronic case of 3 yrs. standing. Partial disability from tender heels and pain in back. No improvement on medicine, baths, etc. Prostate large, tender. Many typical gonococci in prostatic fluid. After each of early injections (300 mil.) pain distinctly worse for 24 hrs. Slow improvement with injections at intervals of 4-5 days. Prostatic message. After 1 month, distinctly better. After 3 months, though not cured decidedly better than for 3 years previously